Obsessive–compulsive disorder in schizophrenia: epidemiologic and biologic overlap

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Objective: To examine the co-existence of obsessive–compulsive disorder (OCD) with schizophrenia in terms of epidemiology and overlapping biologic substrates. **Methods:** Review of the relevant literature. **Results:** There appears to be a significant prevalence of OCD in schizophrenia — higher than what would be expected on the basis of calculated comorbidity figures. There is significant overlap in the proposed functional circuits of OCD and schizophrenia, which may lead to co-expression of symptoms. Although there is overlap in neurotransmitter dysfunction, the interactions are complex, especially in regard to the serotonin and dopamine systems. **Conclusion:** The expression of OCD in schizophrenia is complex but very intriguing. Theoretical hypotheses of the pathology of the 2 disorders now need to be tested in larger controlled trials.

Objectif : Examiner la coexistence de la névrose obsessionnelle et de la schizophrénie sur le plan de l'épidémiologie et des substrats biologiques qui se chevauchent. **Méthodes :** Recension des écrits pertinents. **Résultats :** La névrose obsessionnelle semble prévalente en schizophrénie — plus que l'on ne s'y attendrait en fonction des statistiques calculées sur la comorbidité. Il y a dans le cas de la névrose obsessionnelle et de la schizophrénie un chevauchement important des circuits fonctionnels proposés qui peut entraîner une coexpression de symptômes. Même s'il y a chevauchement de la dysfonction des neurotransmetteurs, les interactions sont complexes, particulièrement en ce qui a trait aux systèmes de la sérotonine et de la dopamine. **Conclusion :** L'expression de la névrose obsessionnelle dans les cas de schizophrénie est complexe mais très intrigante. Il faut maintenant vérifier les hypothèses théoriques de la pathologie des 2 troubles au moyen d'études contrôlées de plus grande envergure.

Introduction

There has recently been renewed interest in the overlap between schizophrenia and obsessive–compulsive disorder (OCD), due in part to reports of the emergence of obsessive–compulsive symptoms after atypical antipsychotic pharmacotherapy, and the subsequent attempts to explain this phenomenon. This article provides a general overview of this overlap to aid in better understanding the complex sub-

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group of patients with both OCD and schizophrenia. First, the epidemiology of OCD in schizophrenia will be discussed, followed by a discussion of the biologic similarities between these illnesses — specifically theories concerning functional circuitry and neurotransmitters.

Epidemiology

Obsessions and compulsions are not new symptoms to schizophrenia, nor are psychotic symptoms new to OCD. In a review of French literature of the 19th century, Berrios[1] found reports of patients with both psychotic and obsessive–compulsive symptoms. In a German report published in 1926, obsessive symptoms were found to occur in just over 1% of patients with schizophrenia.[2] Before the introduction of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), other studies attempted to quantify the incidence of obsessive symptoms in schizophrenia as well as to delineate prognostic variables, with contradictory results.[3-7] One could criticize this early work for a lack of defined symptom criteria and rating scales, but this would overshadow the fact that co-existing obsessive–compulsive and psychotic-like symptoms did exist and were reported before the advent of modern neuroleptics and diagnostic manuals.

There are 2 approaches to examining the epidemiology of OCD in schizophrenia: (1) of probands with schizophrenia, what is the percentage with obsessive–compulsive symptoms? (2) of probands with OCD, what is the percentage with psychotic symptoms? Recent studies are limited and have varied methodology in data acquisition, control of variables (including medication) and numbers of subjects. It is not surprising, then, that one finds inconsistencies in reported rates.

Rosen's[5] chart review found that 3.5% of 848 patients with schizophrenia had significant obsessions and compulsions; interestingly, outcomes measures showed that these patients may have had a less severe form of schizophrenia. In another chart review using DSM-III criteria, Fenton and McGlashan[8] found that 12.9% of 163 schizophrenic patients had OCD, although, in contrast to Rosen, they felt that the coexistence led to a worse outcome in schizophrenia. Chart reviews rely on the recognition and documentation of the symptoms by the treating physician, though, which may lead to under-reporting of symptoms.

To correct for the weaknesses of chart review, Berman et al[9] interviewed directly the therapists of 108 patients with schizophrenia and found that 25% had significant obsessive–compulsive symptoms. Eisen et al,[10] using a strict protocol that included DSM-III-R criteria and Yale-Brown Obsessive Compulsive Scale (YBOCS) scores for obsessions that were defined as "persistent unwanted ideas not related to their delusions," found that 7.8% of 77 patients also met the criteria for OCD. Although the patients were receiving neuroleptic medication, the type and dosage were not reported. These authors also found that there were no apparent differences in variables such as gender, work status, number of admissions or age of onset between the group with a sole diagnosis of schizophrenia and the group with schizophrenia and OCD. In a recent abstract, Fabisch et al[11] found that, in 42 patients who met the DSM-IV criteria for schizophrenia, the 19% who showed obsessive–compulsive symptoms were more likely to have negative symptoms than positive symptoms of schizophrenia. Another recent abstract found that 26% of patients with schizophrenia met the full criteria for OCD according to DSM-IV, and another 46% had "clinically significant" obsessive–compulsive symptoms.[12]

The other epidemiologic approach to examining OCD and schizophrenia involves patients who are first given a diagnosis of OCD. In past retrospective chart-review studies of patients with OCD, incidence rates of psychotic symptoms ranged from 0.7% to 12.3%.[13-17] In a more recent study, Eisen and Rasmussen[18] found that, of 475 probands with OCD, 14% had significant psychotic symptoms and 4% met the full criteria for schizophrenia. They also documented that the individuals with both OCD and psychotic symptoms were more likely to be single, male and younger at first contact, as well as to have a deteriorative course. Thomsen and Jensen,[19] in a slightly different approach, found that, of 135 patients with a first-time psychiatric admission with a diagnosis of OCD, 5% were later given a diagnosis of schizophrenia. Of the 82 patients with obsessive–compulsive personality disorder, only 1% later received a diagnosis of schizophrenia.

In a community sample, the 1988 National Institute for Mental Health Epidemiologic Catchment Area Study reported a 12.2% rate of comorbidity between OCD and schizophrenia,[20] while Bland et al[21] reported a rate of 59.2% for obsessive–compulsive symptoms in schizophrenia. The main difference between these 2 large community samples was the reporting of obses-

sive–compulsive symptoms versus disorder.

Thus, it appears that OCD and schizophrenia coexist more often than one would expect, based on the illnesses' separate lifetime prevalence rates (1% to 1.5% for schizophrenia, 2% to 3% for OCD[20,21]). Aubrey Lewis, who in the 1930s investigated obsessional illness, stated, "The surprising thing here is not that some obsessionals become obviously schizophrenic, but that only a few do so."[22] To aid in understanding this overlap, one needs to examine the biologic evidence and the theories of both illnesses.

Functional circuits

There have recently been significant gains in the understanding of structural and functional abnormalities in both OCD and schizophrenia. New literature on multiple cortical-subcortical pathways in both diseases may be able to explain theoretically some of the overlap in symptom expression.

It is generally recognized in the literature that there are 3 circuits that include discrete areas of the prefrontal cortex: the dorsolateral prefrontal cortex (DLPFC), the lateral orbital cortex and the anterior cingulate cortex.[23–26] These circuits share anatomic substrates, including the frontal lobe, striatum, globus pallidus and thalamus. Projections from an anatomic region appear to maintain segregation to discrete parts of subsequent anatomic structures in the circuit, maintaining the concept of parallel circuits. However, it is argued that there are open (projections to and from anatomic structures outside the defined circuit) as well as closed (limited to structures of the defined circuit only) properties of these circuits.[23,27,28] The DLPFC circuit has been associated with schizophrenia and the lateral orbital cortex circuit with OCD.

Proposed OCD functional circuit

Modell et al[29] put forth a functional circuit for OCD that included an orbitofronto-striatal-pallido-thalamic pathway. It was thought that problems in modulation of this circuit resulted in obsessive–compulsive symptoms. This hypothesis was supported by the finding that OCD improves with ablation surgery of the orbitofrontal area or the midline thalamic nuclei. Chiocca and Martuza[30] further separated this circuit by stating that the obsessive–compulsive symptoms derived from abnormalities of the above and the anxiety component from alterations of the more traditional Papez circuit. Other lines of evidence supporting this corticostriatal pathway included findings by Talairach et al[31] that stimulation of the cingulate cortex induces stereotypic motions typical of compulsions. Of the most successful surgical operations for OCD, the limbic leukotomy combines bilateral cingulate lesions with lesions in the orbitalmedial frontal area, which contains fibres of the fronto-caudate-thalamic pathway.[32]

Cummings[23] further specifies that this OCD circuit arises in the orbital cortex (Brodmann's area 10) and projects primarily to the ventromedial area of the caudate nucleus, then the globus pallidus, ventro-anterior and mediodorsal thalamus, and back to the cortex. He also describes an orbitofrontal syndrome arising from major insults to this area of the cortex, such as rupture of anterior communicating arteries, orbitofrontal tumours and infarctions. This syndrome includes personality changes as well as behaviours that "reflect an enslavement to environmental cues with automatic imitation of the gestures and actions of others or enforced utilization of objects in the environment."

The present functional theory of this OCD circuit is that increased excitatory output from the orbitofrontal/cingulate cortex, or increased caudate activity, causes inhibition of the dorsal thalamus, which in itself can lead to increased activation of the cortex due to loss of inhibition (Fig. 1).[33]

Evidence of dysfunction of the anatomic substrates of this OCD circuit has been documented. In structural imaging conducted in patients with OCD, caudate volumes are noted to be smaller than usual, but this finding is not consistent.[34–36] More consistency is observed in functional imaging of the basal ganglia, where metabolism or blood-flow abnormalities are documented.[37–40] Rauch et al[41] emphasize the role of the basal ganglia in regard to OCD. They discuss that the putamen is involved with motor functions, while the caudate is thought to influence cognitive functions. The caudate can then be subdivided based on projections from the cortex. The ventral medial caudate is thought to receive projections from the orbital, entorhinal and temporal cortex, while the dorsolateral caudate receives projections from the DLPFC. These researchers believe that abnormalities of the caudate affect attentional shifting — loss of which would explain the "stuck" feeling that people with OCD relate. It has been argued that the basal ganglia is the primary site of pathology, while others believe the primary site is in

the cortex, cingulum or even the thalamus, where functional studies have shown abnormalities, but to a lesser extent and consistency than in other sites.[37,39,43]

In treatment studies it has been shown that, following successful pharmacologic or behavioural treatment, there is a "normalization" in regional cerebral blood flow or metabolism to the caudate, orbitofrontal cortex, cingulate and even the thalamus.[33,42]

The thalamus is an interesting component of this circuit. It appears to play an important role in filtering or "gating" sensory and motor information and, thus, in behaviour modification. The multiple nuclei that constitute the thalamus have many diffuse projections to and from various regions of the cortex. Similar to the caudate, the dorsal nucleus projects to the orbitofrontal region and the mediodorsal to the prefrontal cortex, although significant overlap exists.[25,26] In the literature, the thalamus has been investigated in both OCD and schizophrenia. Thalamic degenerative diseases and infarctions have been known to produce behaviours similar to those produced by frontal lobe disease, including impaired insight, apathetic and disinhibited behaviour, as well as decreased verbal fluency, poor memory and distractibility.[44,45]

Proposed schizophrenia functional circuit

In schizophrenia, a similar circuit, the DLPFC circuit, shares anatomic substrates similar to those of the OCD orbitofrontal circuit (Fig. 1). Although it is discussed less in the literature than the OCD orbitofrontal circuit, Cummings[23] defined a DLPFC circuit that originates in the prefrontal cortical area (Brodmann's areas 9 and 10) and projects primarily to the dorsolateral head of the

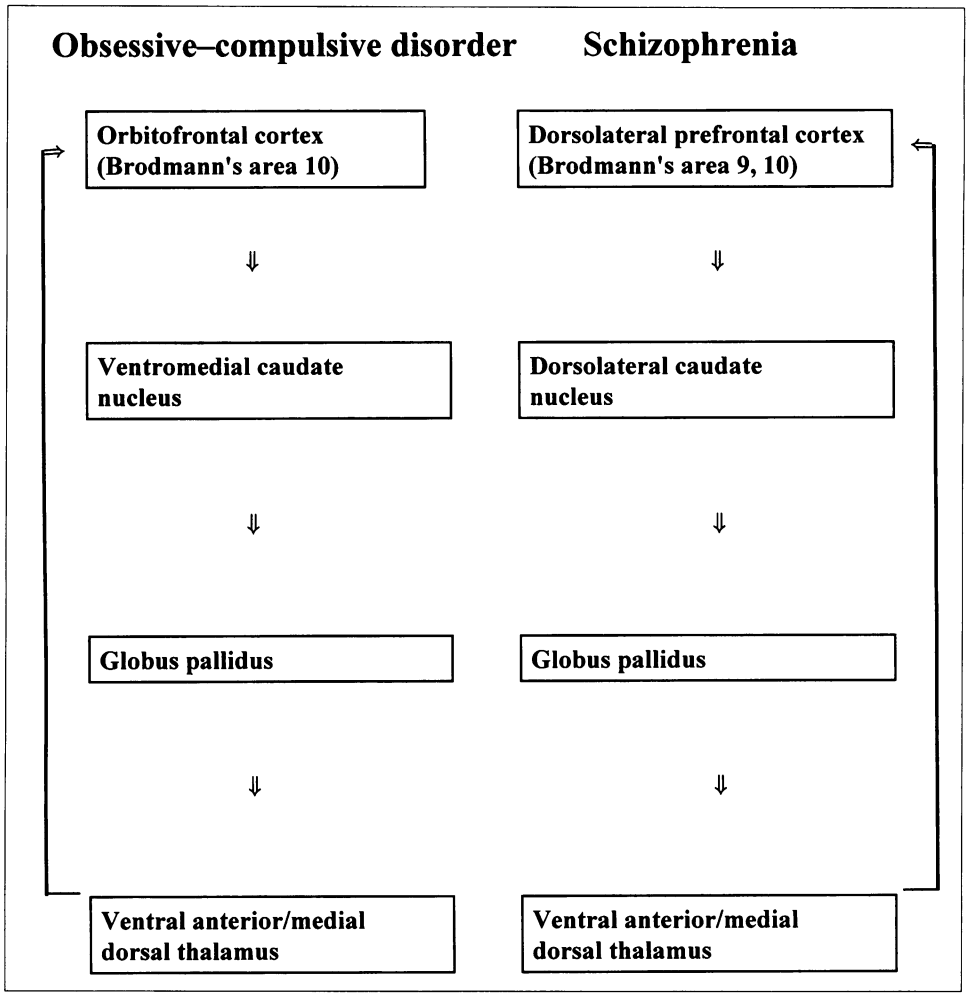

Fig. 1: Functional circuits in obsessive–compulsive disorder and schizophrenia.

caudate (versus ventromedial head in OCD), the globus pallidus, the ventro-anterior and mediodorsal thalamus (as in OCD) and back to the DLPFC. A dorsolateral prefrontal syndrome has been well described; in this syndrome, lesions to the DLPFC have been shown to cause executive functioning abnormalities.

Evidence of anatomic dysfunction in this circuit includes well-documented DLPFC abnormalities. This includes failure of activation of the DLPFC, structural differences in volumes, and membrane composition.[46–48] Recent work has now centred on the thalamus.

Andreasen et al[49,50] and Flaum et al[51] have reported structural abnormalities of the thalamus — specifically, decreased size — in patients with schizophrenia. Positron-emission tomography has shown abnormalities of the thalamus during memory tasks in schizophrenia.[52,53] It is argued that the thalamus filters out unnecessary information and forwards on only relevant information. Deficits in this process may lead to positive symptoms. Andreasen[53] also constructs a prefrontal-thalamic-cerebellar-prefrontal pathway to explain the symptoms of schizophrenia. While there are many more excellent theories in schizophrenia to consider, this idea of "input overload" sounds very similar to that proposed for OCD.

Therefore, more similarities than differences emerge when one examines the parallel development of functional-circuit theory in OCD and schizophrenia. Anatomically, there is significant overlap in structures and substructures. If one accepts that there is an element of open circuitry, thus allowing connections between the various substructures (i.e., between the nuclei of the thalamus) then one could argue that the circuits described for OCD and schizophrenia are very much the same. Similarities between OCD and schizophrenia also emerge if one considers the gating or filtering of sensory information as playing a role in either illness. The fact that similar anatomic structures and parallel cortical–subcortical pathways have been independently documented for both illnesses raises the possibility that a common functional aberration can lead to the co-expression of what appear to be completely different symptoms. This is not to say that all patients with schizophrenia and with OCD share these aberrations, but it helps explain the subgroup of patients that do share these symptoms and the relative frequency of concurrent symptoms. In fact, it seems more plausible that these symptoms can coexist than not.

Neurotransmitters

Serotonin system

Explaining the co-existence of psychotic and obsessive–compulsive symptoms with a simple neurotransmitter hypothesis is formidable. In considering both these illnesses, one has to take into account the relative contributions of the dopamine, serotonin, norepinephrine and γ-aminobutyric acid (GABA) projections and receptor subtypes, as well as their clinical relevance. This task is outside the scope of this article, although some important considerations will be highlighted.

The investigations of the role of serotonin and dopamine in the pathogenesis of OCD and schizophrenia arose from the recent ability to define what successful pharmacologic treatment actually does at the receptor and molecular level. By working backward, hypotheses of dysfunction at the neurotransmitter level in these illnesses were proposed. Although etiology and therapeutics are 2 different issues, they have historically been intertwined.

While the dopamine system has been investigated quite thoroughly in schizophrenia, the research on its possible role in OCD has been limited. This is in contrast to investigations into the serotonin system, which is thought to play a major role in OCD and is now considered to have a role in schizophrenia, owing, in part, to the efficacy of the atypical neuroleptics. In this section, we will focus on the serotonin system, and its relation to the dopamine system, to try to explain the occurrence of OCD in schizophrenia.

On initial inspection, the raphe nuclei appear to project serotonin neurons diffusely throughout the brain but, similar to the functional circuits, there is differentiation. The dorsal raphe project mainly to the cortex and striatum, with fine axons that are particularly associated with the $(5\text{-HT})_2$ receptor subtype and quite sensitive to $(5\text{-HT})_{1A}$ agonists. This differs from the projections of the median raphe, which are beaded axons and project mainly to the hippocampus and septum.[54,55] With respect to the cortex, it is interesting that serotonin innervation is thought to be significantly greater than that of dopamine or norepinephrine.[54–56]

Of the serotonin receptor subtypes, the $(5\text{-HT})_{1A}$ and $(5\text{-HT})_2$ receptors have been most widely investigated in the psychiatric literature. The $(5\text{-HT})_{1A}$ receptor is both pre- and postsynaptic; however, it is the presynaptic autoreceptor that is thought to contribute to reg-

ulation of the firing rate of serotonergic neurons.[57] The $(5\text{-HT})_{1A}$ postsynaptic receptor appears to be limited to the areas of the limbic region, while the $(5\text{-HT})_2$ receptor is found predominately postsynaptically in the cerebral cortex and, to a lesser extent, in areas of the amygdala, cingulate and hypothalamus.[58] Although serotonin neurons with either of the serotonin receptor subtypes project to the cortex, the distribution is stratified. Autoradiographic studies have indicated that $(5\text{-HT})_{1A}$ receptors are concentrated in the external layers of the frontal cortex, while $(5\text{-HT})_2$ receptors are concentrated in layers III and IV.[59]

As well, within the serotonin receptor subtypes there appears to be functional modulation, such that activity at one serotonin receptor subtype affects activity at another. In animals, it has been demonstrated that the $(5\text{-HT})_{1A}$ receptor inhibits $(5\text{-HT})_2$ receptor-mediated behaviour (e.g., head-twitch response in rodents).[60–62] Although less consistent, a possible reciprocal inhibition of $(5\text{-HT})_{1A}$ by $(5\text{-HT})_2$ receptors may occur, as shown by the modulation of the $(5\text{-HT})_{1A}$-mediated ear-scratch response in mice by $(5\text{-HT})_2$ agonists.[61,63]

One can only start to appreciate the complexities involved with the serotonin neurotransmitter system, let alone the interactions with the other neurotransmitters. However, as with the overlap in the anatomic substrates in the functional circuits, there is also possible overlap of neurotransmitter pathology in OCD and schizophrenia.

Dopamine system

Of relevance to this discussion are the interesting interactions between serotonin and dopamine. It has been shown that, via $(5\text{-HT})_2$ postsynaptic receptors on dopamine neurons, serotonin can both inhibit firing rates and decrease dopamine levels in the midbrain (i.e., striatum) and the cortex.[64] Thus, agents that cause a relative increase in serotonin levels, such as serotonergic agonists, serotonin precursors and selective serotonin reuptake inhibitors (SSRIs), enhance the inhibition of the dopamine system within regions of the brain. Conversely, $(5\text{-HT})_{1A}$ agonists and $(5\text{-HT})_2$ antagonists, by decreasing serotonin levels and firing, disinhibit the dopamine system. An interesting primate study involving positron-emission tomography demonstrated this interaction.[65] The researchers were able to show that altanserin, a $(5\text{-HT})_2$ antagonist, increased the release of dopamine, while citalopram, an SSRI, decreased the release of dopamine.

OCD symptoms show improvement as a result of serotonergic agents, including clomipramine and SSRIs, and there are indicators of serotonergic dysfunction in OCD, which, although not specific to this diagnosis, support a serotonin-dysfunction hypothesis. Less robust is the role of dopamine abnormalities in OCD. In animal models of compulsive behaviours, Pittman et al[66] hypothesize that basal ganglia hyperdopaminergic states may underlie compulsions. This finding is in keeping with the basal ganglia abnormalities reported in functional imaging studies to date. One could assume that, as a result of the high concentration of dopamine neurons in the basal ganglia, these abnormalities reflect a primary dopamine pathology in OCD. However, the abnormalities could also represent a result of abnormalities elsewhere, including the serotonin system, especially in light of the influence of the serotonin system on dopamine. Dopamine-blocking medications have been beneficial in OCD-related disorders, including Tourette's syndrome, and in some subpopulations of patients with OCD, in whom antipsychotics have recently been administered as an augmentation strategy.[67–69]

In schizophrenia, the efficacy of typical antipsychotics, which are primarily dopamine D_2-receptor blockers, led to the investigation of dopamine abnormalities in schizophrenia. The success of atypical neuroleptics — which are now known to be less dopamine D_2-receptor blockers and more $(5\text{-HT})_2$-receptor blockers — have shifted this focus. As mentioned previously, the serotonin receptor blockade, which may ultimately disinhibit dopamine in the frontal cortex, may be clinically effective in ameliorating negative symptoms of schizophrenia. Attention is now being focused on the $(5\text{-HT})_2$/dopamine antagonist "ratios" in the development of new antipsychotics.

Thus, again, there is the possibility of significant overlap in the pathology of schizophrenia and OCD, particularly with reference to neurotransmitters. Related to this overlap are the recent reports of the emergence of OCD in patients with schizophrenia who are receiving the newer antipsychotic medications.

Medication-induced OCD in schizophrenia

Recent attention has focused on case reports of spontaneous production of OCD symptoms in patients with chronic schizophrenia who were started on atypical

antipsychotics. To date, 18 such cases have been reported in connection with clozapine, 4 with risperidone and 1 with clothiapine (Table 1).[70–84] While this number of reported cases seems small in comparison with the number of people taking these medications worldwide, it is an interesting phenomenon. These reports most likely led to the 1 prospective study of olanzapine that showed no increase in OCD symptoms in a group of patients with chronic schizophrenia.[85]

The emergence of OCD in patients with schizophrenia receiving atypical antipsychotics could be related to the serotonin and dopamine interactions of these compounds, particularly the $(5\text{-HT})_2$/dopamine antagonist ratios. The ratio of $(5\text{-HT})_2/D_2$ receptor binding affinities for clozapine is twice that for risperidone and clothiapine, and this relation has been hypothesized to explain the higher rate of obsessive–compulsive symptoms observed in patients taking clozapine.[86]

However, these interactions cannot completely explain this phenomenon, since the SSRIs themselves — a treatment for OCD — are $(5\text{-HT})_2$ antagonists. Also of interest, Dursum and Revely[87] have found that long-term clozapine treatment can result in denervation supersensitivity of the $(5\text{-HT})_{2C}$ receptor. This receptor is found in higher concentrations in the basal ganglia than the $(5\text{-HT})_{2A}$ receptor,[88] and, as the basal ganglia are hypothesized to play a key role in OCD, perhaps this phenomenon could be explained at the level of the receptor subtypes. This very interesting area warrants more systematic studies to delve into this further.

Future considerations

OCD in schizophrenia is quite interesting, both from a phenomenologic viewpoint and a biologic and pharmacologic one. Future research in this area has to address such issues as the most appropriate rating scales to use. The YBOCS[89] is the most commonly used rating scale for assessing severity of illness and change in symptoms in OCD. It incorporates a checklist of common obsessions and compulsions, which is useful clinically. The scale is also designed to measure the severity of illness through assessing resistance and interference on 5 parameters; however, this assessment is quite sub-

Table 1: Case reports of antipsychotic-induced obsessive–compulsive disorder (OCD) in schizophrenia

Study	Patient age, sex	Diagnosis	Medication (total daily dose)
Patil, 1992[70]	24, M	Schizophrenia	Clozapine (Not stated)
	34, M	Psychosis	Clozapine (Not stated)
Baker et al, 1992[71]	35, M	Schizophrenia	Clozapine (725 mg)
	33, M	Schizophrenia	Clozapine (700 mg)
	41, F	Schizophrenia	Clozapine (750 mg)
	35, M	Schizophrenia	Clozapine (400 mg)
	39, M	Schizophrenia	Clozapine (575 mg)
Cassady and Thaker, 1992[72]	39, M	Schizophrenia	Clozapine (800 mg)
Patel and Tandon, 1993[73]	30, F	Schizophrenia	Clozapine (400 mg)
	32, F	Schizophrenia	Clozapine (300 mg)
Eales and Layeni, 1994[74]	32, F	Schizophrenia	Clozapine (250 mg)
Buckley et al, 1994[75]	42, M	Delusional disorder	Clozapine (500 mg)
Mozes et al, 1994[76]	10, M	Schizophrenia	Clozapine (275 mg)
Ghaemi et al, 1995[77]	44, M	Schizophrenia and OCD	Clozapine (700 mg)
	36, M	OCD and MAD with psychotic features	Clozapine (150 mg)
Allen and Tejera, 1994[78]	46, M	Schizophrenia	Clozapine (350 mg)
Levkovich et al, 1995[79]	15, M	Schizophrenia	Clozapine (400 mg)
	16, M	Schizophrenia	Clozapine (450 mg)
Remington and Adams, 1994[80]	56, M	Schizophrenia	Risperidone (5 mg)
Kopala and Honer, 1994[81]	22, M	Schizophrenia	Risperidone (6 mg)
Alzaid and Jones, 1997[82]	38, F	Schizophrenia	Risperidone (6 mg)
Dodt et al, 1997[83]	46, M	Schizophrenia	Risperidone (12 mg)
Toren et al, 1995[84]	8, M	Schizophrenia	Clothiapine (10 mg)

jective and provides an estimate of severity only. As well, the concept of resistance and interference may be difficult for a patient with schizophrenia to understand. Thus, the checklist part of the YBOCS would be useful in assessing patients with schizophrenia to rule out obsessions and compulsions, whereas the resistance/interference scores may not be as useful. Other rating scales, such as the Maudsley Obsessional Inventory,[90] may be more useful, or new OCD scales may have to be developed to quantify severity in schizophrenia.

The phenomenon itself is complicated by the fact that DSM-IV includes the specifier "lacking insight" under OCD. It states that this specifier can be used "if for most of the time during the current episode, the person does not recognize that the obsessions and compulsions are excessive or unreasonable." This can cloud the boundaries of what is an obsession: an overvalued idea versus a delusion. If on presentation someone fears that harm will come to a family member if he or she steps on a sidewalk crack and is "lacking insight" into this thought, is this a delusion or an obsession? This theoretical construct remains fuzzy and would benefit from clarification, which would then aid clinical diagnosis and treatment strategies. Clarification would also help address the question of whether OCD symptoms in schizophrenia can be considered a subclass of schizophrenia, or on a continuum of obsessions to compulsions, or just a reflection of comorbidity of 2 psychiatric illnesses.

Further biologic investigations, using larger sample sizes, and tools that are now being used separately in OCD and schizophrenia research, would be extremely beneficial in addressing this question. These tools include neuroimaging (positron-emission tomography, single-photon emission computed tomography, magnetic resonance imaging), family studies, and pharmacologic research.

Patient with concurrent OCD and schizophrenia constitute a very intriguing group of individuals. Researchers in both OCD and schizophrenia are needed to unravel the complexities of this co-occurrence phenomenon. The initial biologic theories of co-existence of obsessive–compulsive symptoms and psychotic symptoms now need to be expanded and tested.

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